(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
13 February 2003 (13.02.2003)

PCT

(10) International Publication Number
WO 03/011352 A1

(51) International Patent Classification[7]: A61L 15/42, 15/60

(21) International Application Number: PCT/GB02/03406

(22) International Filing Date: 25 July 2002 (25.07.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
0118250.0 26 July 2001 (26.07.2001) GB

(71) Applicant *(for all designated States except US)*: **JOHSON & JOHSON MEDICAL LIMITED** [GB/GB]; Erskine House, 68-73 Queen Street, Edinburgh EH2 4NH (GB).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **CULLEN, Breda, Mary** [GB/GB]; 7 Consort Street, Skipton, North Yorkshire BD23 1HR (GB). **KIRKWOOD, Andrew, James** [GB/GB]; 19 Stephensons Walk, Cottingham, Hull, East Yorkshire HU16 4QG (GB).

(74) Agents: **JAMES, Anthony, Christopher, W., P.** et al.; Carpmaels & Ransford, 43 Bloomsbury Square, London WC1A 2RA (GB).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 03/011352 A1

(54) Title: APERTURED SHEET MATERIALS CONSISTING OF A HYDROGEL COMPOSITION

(57) Abstract: A self-supporting apertured sheet consisting essentially of a water-swellable hydrogel composition, wherein the area of the apertures is up to about 50 % of the area of the sheet before swelling. Also provided are wound dressings comprising such sheets. Also provided is a method of making such sheets comprising the steps of: providing an apertured substrate sheet; coating an aqueous hydrogel precursor onto the apertured substrate; curing the aqueous hydrogel precursor on the substrate to form an apertured hydrogel layer on the substrate sheet; and separating the apertured hydrogel layer from the substrate sheet.

APERTURED SHEET MATERIALS CONSISTING OF A HYDROGEL COMPOSITION

The present invention relates to apertured, water-swellable sheet materials and to wound dressings comprising such sheet materials.

It is known that the maintenance of a moist wound environment promotes the healing of wounds, especially burns and chronic wounds such as ulcers. However, it is also desirable to avoid excessive moisture or pooling of wound exudate on the wound, since liquid exudate causes maceration of skin adjacent to the wound and other difficulties. Furthermore, liquid exudate can leak from the wound site and contaminate clothes or bedding.

In practice, it is difficult to maintain the desired moisture level at the wound site because the rate of wound fluid production varies from wound to wound, and over time for any single wound. This can necessitate frequent dressing changes and a range of dressing types to treat different wounds.

EP-A-0123465 describes the use in surgical dressings of continuous polymer films formed from materials that have a higher moisture vapor permeability when the film is wet than when the film is dry.

EP-A-0875222 describes wound dressings comprising a non-swelling, water-impermeable apertured sheet having slits cut therein, wherein the apertured sheet is laminated to a water swellable foam layer. Absorption of wound fluid causes the foam layer to swell, and the resulting deformation opens the slits in the apertured sheet thereby increasing the liquid permeability of the apertured sheet.

EP-A-0122085 describes wound dressings having a apertured sheet of water swellable material laminated to a less water-swellable layer. Slits are cut in the apertured sheet. In use, differential swelling of the apertured sheet and the underlying layer causes the slits in the apertured sheet to open, thereby increasing the permeability of the apertured sheet to wound fluid.

US-A-5352508 describes an apertured substrate web coated with a hydrogel material for use in wound dressings.

It has now been found that certain apertured, self-supporting hydrogel sheets undergo swelling in water to produce water-swelled sheets having greater liquid permeability than the unswelled sheets. This is thought to be due to an increase in the average area of the apertures due to the swelling.

Accordingly, the present invention provides a self-supporting apertured sheet consisting essentially of a water-swellable hydrogel composition, wherein the apertures make up less than 50% of the area of the sheet before swelling.

Typically, the apertures make up from about 0.1% to about 50% of the area of the sheet (preferably of the wound facing area of the sheet) before swelling, more typically from about 1% to about 30% of the area of the sheet before swelling, preferably from about 10% to about 25%, and more preferably from about 10% to about 20%. of the area of the sheet before swelling.

The apertured hydrogel sheet enables a moist wound environment to be maintained for prolonged periods, over a wide range of wound exudation rates. When the exudation rate is high, the apertured sheet expands and the resulting increase in the size of the apertures increases their liquid permeablility. The sheet is thereby able to wick away wound fluid to prevent excessive moisture in the wound without removal of the hydrogel or blocking of the apertures in the hydrogel. When the rate of wound exudate production falls, the hydrogel sheet shrinks and the resulting drop in liquid permeability helps to retain wound fluid at the surface of the wound. Furthermore, the hydrogel absorbs moisture vapor and functions as a humectant to preserve a moist wound contacting surface.

In certain embodiments, the area of the apertures is increased by at least about 25%, for example at least about 50% by swelling the sheet in water at 25°C for 60 minutes.

Typically, the sheet has from about 1 to about 30 apertures per square cm, for example from about 4 to about 15 apertures per square cm or from about 5 to about 10 apertures per square cm. In certain embodiments the apertures are uniformly distributed over the surface of the sheet, preferably in a regular pattern.

The apertures are preferably small, since this results in the greatest proportional increase in liquid permeability when the hydrogel sheet swells. For example, the mean area of each aperture may be from about 0.01 to about 10 mm^2, preferably from about 0.1 to about 4 mm^2, and more preferably from about 1 mm^2 to about 2 mm^2.

The apertures may have any suitable shape, as long as the size of the apertures increases when the hydrogel swells so as to increase the liquid permeability. In certain embodiments, the apertures before swelling have a ratio of maximum length to maximum width of from about 1 to about 10, preferably from about 1 to about 3, and more preferably from about 1 to about 1.5. Suitable aperture shapes include round, oval or regular polygonal

The cross-section of the apertures may be constant (tubular) through the thickness of the hydrogel sheet. In other embodiments, the apertures may taper through the thickness of the sheet. This can result in apertures substantially in the form of truncated cones. Such apertures allow water to flow more readily in one direction through the sheet than in the opposite direction.

Preferably, such apertures have a base opening dimension (the maximum opening dimension in the top of the apertured sheet) of from 0.1 mm to 3 mm, and an apical opening dimension (remote from the top of the apertured sheet) of from 0.05 to 2 mm. More preferably, the apertures have a base opening dimension as herein defined of from 0.5 mm to 2 mm, and an apical opening dimension of from 0.1 to 1.0 mm.

Preferably, the apertures have an average angle of taper (measured from the perpendicular to the plane of the apertured sheet) of from 10 to 60 degrees.

The apertured hydrogel sheet is self-supporting. That is to say, the apertured sheet does not have any reinforcing or supporting sheet, web, net or member embedded therein or laminated thereto. The apertured hydrogel sheet normally consists essentially of the hydrogel composition as hereinafter described. Naturally, the self-supporting nature of the sheet implies that the hydrogel composition has a minimum inherent strength. Preferably, the hydrogel composition (measured on a continuous strip (2.5 cm wide) of the hydrogel in accordance with ASTM 412) has a breaking force of 0.5- 10 N, more preferably 1-5 N.

Preferably, the thickness of the apertured sheet (by ASTM D374-79) is from about 0.2 to about 4 mm, more preferably from about 0.4 to about 2 mm. Preferably, the hydrogel layer has a dry basis weight of from about 10 to about 1000g/m^2, more preferably from about 20 to about 200g/m^2, and most preferably from about 40 to about 100g/m^2.

The term "water-swellable hydrogel composition" refers to compositions that absorb water to form a gel with water under physiological conditions of temperature and pH. Such compositions comprise medically acceptable macromolecular materials that have the ability to swell and absorb wound fluid while maintaining a strong integral structure. Normally, the hydrogel composition is substantially insoluble in water under physiological conditions, whereby the hydrogel is not washed away by the wound fluid. The hydrogel may comprise a biopolymer, i.e it may be formed from a polymer found in nature such as collagen, gelatin or alginate. The hydrogel may be bioabsorbable. That is to say, it may undergo gradual resorption *in vivo*.

Typically, the apertured sheet according to the present invention absorbs at least about 10% w/w of water preferably at least about 25% w/w of water, more preferably at least about 50% w/w of water, and still more preferably at least about

100% w/w of water on immersion at 25°C for 60 minutes, based on the weight of the sheet before immersion.

Exemplary insoluble gels include certain cross-linked polyacrylate gels such as those described in EP-A-0676457, calcium alginate gels, cross-linked hyaluronate gels, gels of alginate derivatives such as propylene glycol alginate, and gels wherein the hydropolymer is formed from vinyl alcohols, vinyl esters, vinyl ethers and carboxy vinyl monomers, meth(acrylic) acid, acrylamide, N-vinyl pyrrolidone, acylamidopropane sulphonic acid, PLURONIC (Registered Trade Mark) (block polyethylene glycol, block polypropylene glycol) polystyrene-, maleic acid, NN-dimethylacrylamide diacetone acrylamide, acryloyl morpholine, and mixtures thereof. Suitable hydrogels are also described in US-A-5352508.

Preferably, the hydrogel composition comprises a macromolecular material selected from polyurethane gels, biopolymer gels, carboxymethyl cellulose gels, hydroxyethyl cellulose gels, hydroxy propyl methyl cellulose, polyacrylate and mixtures thereof. Suitable biopolymer gels include alginates, pectins, gelatin gels, galactomannans such as guar and xanthan, chitosan, gelatin, hyaluronates and mixtures thereof. Some of these biopolymer materials also promote wound healing.

Preferably, the gels are chemically or physically cross-linked, and the chemical cross-linking may be either covalent or ionic.

The apertured sheet may comprise at least 50% w/w based on the weight of the sheet before swelling of the gel-forming macromolecular materials, more preferably at least 75% w/w. The hydrogel material may further comprise from about 5 to about 50% by weight, preferably from 15 to 40% by weight, on the same basis of one or more humectants such as glycerol. The hydrogel material may further contain up to about 30% w/w, more preferably up to about 15% w/w on the same basis of water.

The hydrogel composition may further comprise up to about 10% w/w, preferably from 0.1% to 5% w/w of a medicament based on the weight of the composition before swelling. Suitable medicaments include antiseptics such as silver sulfadiazine, chlorhexidine, triclosan or povidone iodine, analgesics, steroids, antibiotics, growth factors or mixtures thereof. Preferably, the apertured sheet according to the invention is substantially sterile.

The apertured sheet according to the present invention may in some embodiments be adhesive. In certain embodiments the hydrogel composition of the sheet itself is adhesive. In other embodiments a medically acceptable pressure sensitive adhesive may be applied to a surface of the apertured sheet.

In certain embodiments, the hydrogel layer comprises a cross-linked polyacrylate hydrogel material, for example a material of the kind described in EP-A-0676457, WO00/07638, or WO00/45866, the entire contents of which are incorporated herein by reference.

The present invention further provides a wound dressing comprising an apertured sheet according to the present invention.

Preferably, the wound dressing comprises an absorbent layer and/or a backing layer in addition to the apertured sheet, in which case the apertured sheet is preferably the wound-facing top sheet of the dressing.

Preferably, the dressing further comprises a backing layer over the back face of the apertured sheet. The backing layer preferably provides a barrier to passage of microorganisms through the dressing and further preferably blocks the escape of wound fluid from the dressing. The backing layer may extend beyond at least one edge of the absorbent layer to provide an adhesive-coated margin adjacent to the said edge for adhering the dressing to a surface, such as to the skin of a patient adjacent to the wound being treated. An adhesive-coated margin may extend around all sides of the absorbent layer, so that the dressing is a so-called island

dressing. However, it is not necessary for there to be any adhesive-coated margin.

Preferably, the backing layer is substantially liquid-impermeable. The backing sheet is preferably semipermeable. That is to say, the backing sheet is preferably permeable to water vapour, but not permeable to liquid water or wound exudate. Preferably, the backing sheet is also microorganism-impermeable. Suitable continuous conformable backing sheets will preferably have a moisture vapor transmission rate (MVTR) of the backing sheet alone of 300 to 5000 g/m^2/24hrs, preferably 500 to 2000 g/m^2/24hrs at 37.5 C at 100% to 10% relative humidity difference. The backing sheet thickness is preferably in the range of 10 to 1000 micrometers, more preferably 100 to 500 micrometers.

The MVTR of the dressing according to the present invention as a whole is lower than that of the backing sheet alone, because the apertured sheet partially obstructs moisture transfer through the dressing. Preferably, the MVTR of the dressing (measured across the island portion of the dressing) is from 20% to 80% of the MVTR of the backing sheet alone, more preferably from 20% to 60% thereof, and most preferably about 40% thereof. It has been found that such moisture vapor transmission rates allow the wound under the dressing to heal under moist conditions without causing the skin surrounding the wound to macerate.

Suitable polymers for forming the backing sheet include polyurethanes and poly alkoxyalkyl acrylates and methacrylates such as those disclosed in GB-A-1280631. Preferably, the backing sheet comprises a continuous layer of a high density blocked polyurethane foam that is predominantly closed-cell. A suitable backing sheet material is the polyurethane film available under the Registered Trade Mark ESTANE 5714F.

The adhesive (where present) layer should be moisture vapor transmitting and/or patterned to allow passage of water vapor therethrough. The adhesive layer is preferably a continuous moisture vapor transmitting, pressure-sensitive adhesive

layer of the type conventionally used for island-type wound dressings, for example, a pressure sensitive adhesive based on acrylate ester copolymers, polyvinyl ethyl ether and polyurethane as described for example in GB-A-1280631. The basis weight of the adhesive layer is preferably 20 to 250 g/m^2, and more preferably 50 to 150 g/m^2. Polyurethane-based pressure sensitive adhesives are preferred.

Preferably, the adhesive layer extends outwardly from the absorbent layer and the envelope to form an adhesive-coated margin on the backing sheet around the adhesive layer as in a conventional island dressing.

The area of the optional absorbent layer is typically in the range of from 1cm^2 to 200cm^2, more preferably from 4cm^2 to 100cm^2.

The optional absorbent layer may be any of the layers conventionally used for absorbing wound fluids, serum or blood in the wound healing art, including gauzes, nonwoven fabrics, superabsorbents, hydrogels and mixtures thereof. Preferably, the absorbent layer comprises a layer of absorbent foam, such as an open celled hydrophilic polyurethane foam prepared in accordance with EP-A-0541391, the entire content of which is expressly incorporated herein by reference. In other embodiments, the absorbent layer may be a nonwoven fibrous web, for example a carded web of viscose staple fibers. The basis weight of the absorbent layer may be in the range of 50-500g/m^2, such as 100-400g/m^2. The uncompressed thickness of the absorbent layer may be in the range of from 0.5mm to 10mm, such as 1mm to 4mm. The free (uncompressed) liquid absorbency measured for physiological saline may be in the range of 5 to 30 g/g at 25°

Preferably, the wound dressing according to the present invention is sterile and packaged in a microorganism-impermeable container.

In another aspect, the present invention provides a method of manufacture of an apertured sheet, comprising the steps of:

providing an apertured substrate sheet;

coating an aqueous hydrogel precursor onto the apertured substrate;

curing the aqueous hydrogel precursor on the substrate to form an apertured hydrogel layer on the substrate sheet; and

separating the cross-linked hydrogel layer from the substrate sheet.

The substrate sheet is preferably a perforated thermoplastic film, such as a PTFE film or a polyolefin film or an ethylene vinyl acetate (EVA) film. Preferred are vacuum perforated films, such as the films with tapered apertures described in GB-A-1526778. In other embodiments the substrate sheet may be a perforated metal or plastic plate, or mesh of metal or thermoplastic filaments. In certain embodiments the substrate sheet may be coated with a release coating, such as a silicone release coating, to assist peeling of the apertured sheet product from the substrate.

The hydrogel precursor is a pregel composition that forms an insoluble hydrogel upon cooling, polymerisation or cross-linking. Examples include aqueous sodium alginate, which can be gelled by calcium salts. Another example is guar gum, which can be gelled by borate salts. In other embodiments, the pregels are curable compositions that comprise one or more monomers and typically one or more crosslinking agents and/or polymerisation initiators. Preferred monomers are acrylate esters, such as 2-hydroxyethyl methacrylate, acrylamides such as N,N-dimethylacrylamide. Also preferred are mixtures of salts or C1-C5 esters of 2-acrylamide-2-methylpropanesulfonic acid and salts or C1-C5 alkyl esters of acrylic acid (3-sulfopropyl) ester. Suitable cross linking agents are polyethylene glycol diacrylates. Suitable initiators are conventional peroxide initiators.

Suitable pregel materials are the UV-curable polyacrylate pregels described for example in WO00/65143, the entire content of which is incorporated herein by reference.

Preferably, the viscosity of the pregel is adjusted to provide the desired thickness of the pregel layer on the substrate.

The pregel can be coated onto the substrate surface for example by spraying or slot coating or extrusion or by means of a doctor blade. Apertures may be formed in the pregel coating, for example, by applying a gas pressure differential across the coated substrate to blow apertures in the coating. Methods of this general type are described, for example, in WO93/19709. Alternatively, an apertured hydrogel coating on an apertured substrate may be made by the method described in WO00/65143, the entire content of which is incorporated herein by reference.

The apertured hydrogel sheet is preferably separated from the substrate by peeling.

In a further aspect the present invention provides a method of treatment of a wound comprising the step of applying a dressing in accordance with the present invention to the surface of the wound with the apertured hydrogel sheet contacting the wound.

Specific embodiments of the present invention will now be described further, by way of example.

Example 1

An apertured hydrogel sheet according to the invention is prepared as follows.

A substrate sheet is provided consisting of a polyethylene film that has been perforated with about 10 perforations per cm^2, each perforation having a substantially conical shape as hereinbefore described, a maximum hole diameter of about 1.0 mm, an open area of 16% of the total area of the front face, a thickness by weight of about 43 micrometers and an embossed thickness of about 0.5 mm. Such perforated sheets are available from Tredegar Film Products, Richmond, Virginia under the Registered Trade Mark VISPORE.

The substrate sheet presents a smooth, perforated top surface. This surface is then coated with a layer of hydropolymer pregel 6 that is applied by spraying. The pregel consists of bovine gelatin in water at about 25°C. The concentration of the gelatin is adjusted in the range 5 to 20% w/w to provide the desired viscosity for a uniform, adherent layer of the desired thickness on the substrate. Suction is then applied to the back face of the substrate to vacuum perforate the pregel layer in register with the perforations in the substrate. The gelatin is then cross-linked by treatment with glutaraldehyde or formaldehyde. The cross-linked gelatin sheet is then dried at 40°C and then peeled from the substrate sheet.

The resulting hydrogel sheet has a dry basis weight of 100g/m^2 and consists of bovine gelatin cross-linked with glutaraldehyde or formaldehyde. The sheet has about 10 perforations per cm^2, each perforation having a maximum hole diameter in the range of about 0.8- 1.2 mm, resulting in an open area of about 5-10% of the total area of the apertured sheet. On soaking in water at 25°C for one hour the gelatin swells but does not dissolve, and it can be seen that the holes enlarge, thereby increasing the liquid permeability of the sheet.

The sheet can be packaged directly for use, or it can be made up into a multilayer wound dressing according to the invention. It can be sterilized by gamma irradiation.

In use, the dressing is removed from the package, and the apertured hydrogel sheet is applied to the wound with the hydrogel in contact with the wound to provide a sterile and absorbent dressing. The hydrogel sheet interacts in hitherto unexpected ways to provide a moist but not wet wound environment for a wide range of wounds over an extended period.

Example 2

An apertured sheet formed from a polyvinyl pyrrolidone (PVP) gel according to the invention is prepared from the following pregel formulation

PVP	20%
Water	79.16%
Methyl paraben	0.25%
Ethyl paraben	0.03%
Propyl paraben	0.05%
Butyl paraben	0.01%
2-phenoxyethanol	0.50%

The thus-formed gel solution is then extruded through a slot die onto a substrate sheet of the same kind as in Example 1 moving at a speed of 5 m/minute, at a coating weight of 1000 g/m^2. Suction is applied to perforate the pregel coating as described in Example 1.

The pregel is then cured by passing it through a heating oven at 60 degrees. The resulting cured hydrogel layer is then dried at 40°C and peeled from the substrate.

Example 3

A PTFE mold was prepared with conical projections spaced every 3mm. The projections were 3mm high, and were 2mm diameter at the base and 1mm diameter at the top of the cone. The mold was filled with a polyacrylate monomer solution prepared as follows: 80mls of a solution made from 50% w/v 2-acrylamido-2-methylpropane sulfonic acid; 20mls of water; 5 mls of Potassium Chloride (5%w/v); 0.15ml of a solution prepared from 20 parts PEG400, and 6 parts of 1-hydroxycyclohexylphenylketone.

The monomer solution was polymerised by exposure to UV light, and the polymerised gel was peeled from the mould, to provide a self supporting perforated gel.

The above embodiments have been described by way of example only. Many other embodiments falling within the scope of the accompanying claims will be apparent to the skilled reader.

5

CLAIMS

1. A self-supporting apertured sheet consisting essentially of a water-swellable hydrogel composition, wherein the area of the apertures is up to about 50% of the area of the sheet before swelling.

2. An apertured sheet according to claim 1, wherein the area of the apertures is from about 0.1% to about 50% of the area of the sheet before swelling.

3. An apertured sheet according to claim 1 or 2, having from about 1 to about 30 apertures per square cm.

4. An apertured sheet according to any preceding claim, wherein the mean area of each aperture is from about 0.01 to about 4 mm^2.

5. An apertured sheet according to any preceding claim, wherein the apertures before swelling have a ratio of length to width of from about 1 to about 10.

6. An apertured sheet of a water-swellable material, wherein the area of the apertures is increased by at least 50% by swelling the sheet in water at 25°C for 60 minutes.

7. An apertured sheet according to any preceding claim, wherein the water-swellable hydrogel composition has a tensile strength of 2-5 N in a 2.5 cm wide strip.

8. An apertured sheet according to any preceding claim, wherein the apertures are tapered from a front surface to a back surface of the sheet

9. An apertured sheet according to any preceding claim, wherein the sheet absorbs at least 50% w/w of water on immersion at 25°C for 60 minutes, based on the weight of the sheet before immersion.

10. An apertured sheet according to any preceding claim, wherein the sheet has a dry basis weight of from 10 to 1000 g/m^2.

11. An apertured sheet according to any preceding claim, wherein the sheet has a thickness as determined by ASTM D374-79 of from about 0.2 to about 4 mm.

12. An apertured sheet according to any preceding claim, wherein the sheet material comprises a hydrogel selected from polyurethane gels, gelatin gels, pectin gels, alginate gels, glycosaminoglycan gels, hyaluronic acid gels, guar gels, xanthan gels, gels formed from starch derivatives, carboxymethyl cellulose gels, hydroxyethyl cellulose gels, hydroxypropyl methyl cellulose, polyethylene oxides and mixtures thereof.

13. An apertured sheet according to any preceding claim, wherein the hydrogel layer comprises a hydrogel selected from gels formed by polymerising or copolymerising vinyl alcohols, vinyl esters, vinyl ethers and carboxy vinyl monomers, meth(acrylic) acid, vinyl amide monomers, anionic vinyl monomers, hydroxy vinyl monomers, cationic vinyl monomers containing amines or quaternary groups, ionic acrylamide derivatives, N-alkyl acrylamides, acrylate esters, ionic acrylate ester derivatives, N-vinyl pyrrolidone, acylamidopropane sulphonic acid, maleic acid, NN- dimethylacrylamide, diacetone acrylamide or acryloyl morpholine.

14. An apertured sheet according to any preceding claim, wherein the hydrogel is chemically or physically cross-linked

15. A wound dressing comprising an apertured sheet according to any preceding claim.

16. A wound dressing according to claim 15, further comprising an absorbent layer in contact with a back surface of the apertured sheet.

17. A wound dressing according to any preceding claim, wherein the absorbent layer comprises a layer of hydrophilic foam.

18. A wound dressing according to claim 15, 16 or 17, wherein the dressing further comprises a backing layer over the apertured sheet.

19. A wound dressing according to claim 18, wherein the backing layer is substantially liquid-impermeable.

20. A wound dressing according to claim 18 or 19, further comprising a layer of adhesive on the surface of the backing layer facing the apertured sheet.

21. A wound dressing according to claim 6, wherein the backing layer extends beyond at least one edge of the apertured sheet to provide an adhesive-coated margin adjacent to said edge for adhering the dressing to a surface.

22. A wound dressing according to any one of claims 16 to 21 which is sterile and packaged in a microorganism-impermeable container.

23. A method of manufacture of an apertured sheet according to any one of claims 1 to 22, comprising the steps of:

providing an apertured substrate sheet;

coating an aqueous hydrogel precursor onto the apertured substrate;

curing the aqueous hydrogel precursor on the substrate to form an apertured hydrogel layer on the substrate sheet; and

separating the apertured hydrogel layer from the substrate sheet.

24. A method according to claim 23, wherein the coating of aqueous hydrogel precursor is perforated by applying a gas pressure differential across the coated substrate.

INTERNATIONAL SEARCH REPORT

Inte ..ional Application No
PCT/GB 02/03406

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61L15/42 A61L15/60

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61F A61L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 122 085 A (SMITH & NEPHEW ASS) 17 October 1984 (1984-10-17) cited in the application page 8, line 4-18 page 14, line 1-10 page 17, line 1-6 page 18 -page 19	1-24
A	GB 2 093 703 A (SMITH & NEPHEW ASS) 8 September 1982 (1982-09-08) page 1, line 59-65 page 2, line 16-30,75-82,93-95,105-109	1-24
A	DE 43 08 445 A (BEIERSDORF AG) 22 September 1994 (1994-09-22) page 2, line 3-14 page 6, line 40-46	1,23,24

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the International search report
23 October 2002	31/10/2002

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Böhm, I

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Inte .ional Application No
PCT/GB 02/03406

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	DE 42 42 015 A (SEBAPHARMA GMBH & CO) 7 October 1993 (1993-10-07) column 1, line 3-13	1
A	US 4 909 244 A (HYLA PATRICK H ET AL) 20 March 1990 (1990-03-20) column 3, line 52-59 column 4, line 3-8 claims	1,15
A,P	WO 02 47737 A (JOHNSON & JOHNSON MEDICAL LTD ;SILCOCK DEREK (GB); MARSDEN DONALD) 20 June 2002 (2002-06-20) page 3, line 11-14 page 5, line 23,24 page 6, line 15-20 page 10, line 17-20	1,10,12, 13,15-24
A,P	WO 02 38097 A (JOHNSON & JOHNSON MEDICAL LTD ;ADDISON DEBORAH (GB); SILCOCK DEREK) 16 May 2002 (2002-05-16) page 6, line 8 -page 7, line 6	1

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/GB 02/03406

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
EP 0122085 A	17-10-1984	AT	27904 T	15-07-1987
		AU	564402 B2	13-08-1987
		AU	2644984 A	11-10-1984
		CA	1214085 A1	18-11-1986
		DE	3464326 D1	30-07-1987
		EP	0122085 A1	17-10-1984
		JP	1036380 B	31-07-1989
		JP	1555629 C	23-04-1990
		JP	59205959 A	21-11-1984
		US	4541426 A	17-09-1985
		ZA	8402504 A	30-01-1985
GB 2093703 A	08-09-1982	US	4995382 A	26-02-1991
		US	4860737 A	29-08-1989
		US	4753231 A	28-06-1988
		AT	14523 T	15-08-1985
		AT	16345 T	15-11-1985
		AU	552887 B2	26-06-1986
		AU	8037582 A	19-08-1982
		CA	1174447 A1	18-09-1984
		DE	3264978 D1	05-09-1985
		DE	3267220 D1	12-12-1985
		DK	63882 A ,B,	14-08-1982
		EP	0059048 A1	01-09-1982
		EP	0059049 A1	01-09-1982
		GB	2093702 A ,B	08-09-1982
		IE	52669 B1	20-01-1988
		JP	1654159 C	13-04-1992
		JP	3013902 B	25-02-1991
		JP	57153644 A	22-09-1982
		NZ	199684 A	20-03-1985
		US	5445604 A	29-08-1995
		US	5147338 A	15-09-1992
		ZA	8200933 A	23-02-1983
DE 4308445 A	22-09-1994	DE	4308445 A1	22-09-1994
		AU	692424 B2	11-06-1998
		AU	4820193 A	26-04-1994
		DE	59309311 D1	25-02-1999
		WO	9407935 A1	14-04-1994
		EP	0665856 A1	09-08-1995
		ES	2129082 T3	01-06-1999
		JP	8501819 T	27-02-1996
		US	5844013 A	01-12-1998
DE 4242015 A	07-10-1993	DE	4242015 A1	07-10-1993
		AT	173640 T	15-12-1998
		DE	59309160 D1	07-01-1999
		WO	9319789 A1	14-10-1993
		EP	0633789 A1	18-01-1995
		JP	3252910 B2	04-02-2002
		JP	7508429 T	21-09-1995
US 4909244 A	20-03-1990	NONE		
WO 0247737 A	20-06-2002	GB	2369997 A	19-06-2002
		AU	2216102 A	24-06-2002
		WO	0247737 A1	20-06-2002

INTERNATIONAL SEARCH REPORT

Information on patent family members

Int. ..ional Application No
PCT/GB 02/03406

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0238097 A	16-05-2002	AU 1255202 A	21-05-2002
		WO 0238097 A1	16-05-2002